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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,216	BAKER ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *September 19, 2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's telephonic election made on April 26, 2006.

Claims 1-20 are pending in the instant application.

Claims 15-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. It is noted that SEQ ID NOs: 18-32, 34, 35, 37-49, 51-78, 81-86, 88, 89, 93-96, 98-103, 105-110, 112-120, 122-124, 126-129, 132, 134, 136-147, 149-154, 157-159, 161-164, 166, or 168 as recited in claim 3 are also withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the telephonic election made on April 26, 2006.

Claims 1-14 have been examined on the merits.

Election/Restrictions

The Election/Restriction mailed on November 2, 2005 is withdrawn in view of the new Election/Restriction as detailed below:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-14, drawn to a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound

specifically hybridizes with and inhibits the expression of urokinase plasminogen activator, classifiable in class 536, subclass 24.5.

II. Claims 15-20, drawn to a method of inhibiting the expression of urokinase plasminogen activator or a method of treating an animal having a disease or condition associated with urokinase plasminogen activator, classifiable in class 435, subclass 375 and class 514, subclass 14.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I and Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product compound of Group I can be used as a hybridization probe in a method of detecting urokinase plasminogen activator gene expression, which is materially different than the method of inhibiting expression of a gene encoding urokinase plasminogen activator or a method of treating an animal having a disease or condition associated with urokinase plasminogen activator of Group II. Furthermore, restriction is proper because the subject matter is divergent and non-coextensive and a search for one Group would not necessarily reveal art against the other Group. It is therefore a burden to search both of these inventions in a single application.

Claim 3 is subject to an additional restriction since it is not considered to be a proper genus/Markush. See MPEP 803.02 - PRACTICE RE MARKUSH-TYPE CLAIMS - If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claim 3 specifically claims urokinase plasminogen activator antisense SEQ ID NOs: 18-35, 37-49, 51-78, 81-86, 88, 89, 93-96, 98-103, 105-110, 112-120, 122-124, 126-129, 132, 134, 136-147, 149-154, 157-159, 161-164, 166, or 168, which are targeted to and modulate the expression of urokinase plasminogen activator. Although the antisense sequences claimed each target and modulate expression of urokinase plasminogen activator, the instant antisense sequences are considered to be unrelated, since each antisense sequence claimed is structurally and functionally independent and

distinct for the following reasons: each antisense sequence has a unique nucleotide sequence, each antisense sequence targets a different and specific region of a urokinase plasminogen activator nucleic acid, and each antisense, upon binding to a urokinase plasminogen activator nucleic acid, functionally modulates (increases or decreases) the expression of the gene and to varying degree (per Applicant's Tables 1 and 2 in the specification). As such the Markush/genus of antisense sequences in claim 3 is not considered to constitute a proper genus, and is therefore subject to restriction. Furthermore, a search of more than one (1) of the antisense sequences claimed in claim 3 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed antisense sequences. In view of the foregoing, one (1) antisense sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect one (1) antisense sequence from claim 3. Note that this is not a species election.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one

or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephonic conversation with Frances Putkey and Examiner Terra Cotta Gibbs on April 26, 2006, in response to the Election/Restriction as detailed in the instant Action, Applicants elected Group I, claims 1-14 drawn to a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase

plasminogen activator, with traverse. Applicant further elected SEQ ID NO:33 as required in the further restriction as detailed for claim 3. Applicant must make affirmation of this election in replying to this Office Action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

Applicant's information disclosure statement filed September 19, 2003 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Priority

Applicant's reference to priority in the first sentence of the specification is acknowledged, however the reference should be updated to reflect applications for patents that have been abandoned.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it recites a compound that "specifically hybridizes", but does not indicate what the compound hybridizes with. It is unclear whether the compound hybridizes with a nucleic acid molecule encoding urokinase plasminogen activator, or with a protein product of a nucleic acid encoding urokinase plasminogen activator, or any other cellular product. Claims 2-10 and 12-14 are indefinite for the same reasons above, due to their dependence on claim 1.

It is suggested that the claim state, "a nucleic acid molecule encoding urokinase plasminogen activator".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, and 4-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The subject matter of the instantly claimed invention is drawn to a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase plasminogen activator, and to chemical modifications and pharmaceutically acceptable diluents thereof.

The specification teaches a series of antisense oligonucleotides targeted to human urokinase plasminogen activator (Genbank Accession Nos. M15476 and X02419, as represented by SEQ ID NOs: 3 and 17, respectively, in the instant application). The specification also teaches a series of antisense oligonucleotides targeted to mouse urokinase plasminogen activator (Genbank Accession Nos. X02389 and M17922, as represented by SEQ ID NOs: 10 and 90, respectively, in the instant application). However, neither the instant specification, nor the prior art describe compounds targeted to and inhibit the expression of other urokinase plasminogen activator genes, other than the above sequences listed.

At the outset, it is noted that the rejected claims do not recite any sequence identifier relating to urokinase plasminogen activator. This sequence is thus considered to be defined by its function (i.e. the activity of urokinase plasminogen activator) rather than by any one specific structure. Accordingly the claims embrace compounds targeted to urokinase plasminogen activator, or any such molecule with analogous urokinase plasminogen activator activity, known or yet to be discovered, along with any

isoform or allele present within this species, or any variant, polymorphic or otherwise, that is within reasonable similarity from these families of proteins that retain urokinase plasminogen activator activity.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof. The representative sample requirement may be satisfied by supplying structural or functional information, or a combination of both, such that one of skill in the art would be satisfied that applicants were in possession of the genus as claimed. Further, the size of the representative sample required is an inverse function of the unpredictability of the art.

See the January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register for the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement. These guidelines state: "[T]o satisfy the written description requirement, a patent specification must describe the claimed invention in

sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention.

Further, See MPEP § 2163, which states "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

In order to synthesize the compounds targeted to urokinase plasminogen activator and practice the methods as claimed, one of skill would first need the sequence of the urokinase plasminogen activator in order to synthesize said compounds. Although the instant specification teaches a series of antisense oligonucleotides targeted to human and mouse urokinase plasminogen activator, the claims embrace antisense compounds directed to *any* sequence of *any* urokinase plasminogen activator, or any such molecule with analogous urokinase plasminogen

activator activity, known or yet to be discovered, along with any isoform or allele present within this species, or any variant, polymorphic or otherwise, that is within reasonable similarity from these families of proteins that retain urokinase plasminogen activator activity. Apart from further experimentation, the skilled artisan would not have been able to predict the structures of the full scope of the claimed oligonucleotides encompassed by the instant invention, particularly in the absence of any teaching by way of structure or reference to active domains or regions. The genus is not immediately envisioned because the genus of compounds targeted to urokinase plasminogen activator is considered to include not only the urokinase plasminogen activator sequences taught in the instant invention, but also any such molecule with analogous urokinase plasminogen activator activity, known or yet to be discovered. However, the distinguishing characteristics of the claimed genus are not considered to be described herein, or in the prior art. Thus, because one of skill in the art could not envision any compounds targeted to urokinase plasminogen activator, other than those described in the instant specification, one of skill would not be convinced that applicants were in possession of any compounds targeted to urokinase plasminogen activator sequences that are heretofore undescribed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 11, 12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by McGuire et al. (Development, 1993 Vol. 118, pages 931-939, Applicant's reference AD on the Information Disclosure Statement filed September 19, 2003).

Claim 1 is drawn to a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase plasminogen activator. Claims 2, 4, 5, 12, and 14 are dependent on claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound is an antisense oligonucleotide; wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage; wherein the modified internucleoside linkage is a phosphorothioate linkage; and a composition comprising a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase plasminogen activator and a pharmaceutically acceptable carrier or diluent, wherein the compound is an antisense oligonucleotide. Claim 11 is drawn to a compound which specifically hybridizes with at least an 8-nucleobase portion of an active site on a nucleic acid molecule encoding urokinase plasmigongen activator.

McGuire et al. disclose a 15-mer antisense phosphorothioate oligonucleotide targeting and centered on the initiation codon of uPA mRNA (also called urokinase plasminogen activator) (see page 932, first column at antisense oligonucleotide

treatment of isolated cells). It is noted that the antisense oligonucleotide disclosed by McGuire et al. was administered to cells *in vitro* in serum free M199 medium and thus constitutes a pharmaceutically acceptable carrier or diluent.

Therefore, McGuire et al. anticipate claims 1, 2, 4, 5, 11, 12, and 14.

Claims 1, 2 and 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Morrissey et al. (Clin. Exp. Metastasis, 1999 Vol. 17, pages 77-85, Applicant's reference AE on the Information Disclosure Statement filed September 19, 2003).

Claims 1, 2, 11, 12, and 14 are as described above in the 35 U.S.C. 102(b) rejection as being anticipated by McGuire et al. Claim 13 is dependent on claim 1 and includes all the limitations of claim 1 with the further limitation being a composition comprising a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase plasminogen activator and further comprising a colloidal dispersion system.

Morrissey et al. disclose a 22 nucleobase long antisense oligonucleotide targeting bases 368-389 of human uPA mRNA which caused inhibition of urokinase plasminogen activator expression in three human esophageal carcinoma cell lines. It is noted that the antisense oligonucleotide disclosed by Morrissey et al. was administered to cells *in vitro* in reduced-serum medium and thus constitutes a pharmaceutically acceptable carrier or diluent. It is further noted that oligonucleotide uptake by cells was

facilitated by complexing with the cationic lipid transfection reagent DOTAP and thus constitutes a colloidal dispersion system.

Therefore Morrissey et al. anticipate claims 1, 2 and 11-14.

Claims 1, 2, 4, 5, 11, 12, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilhelm et al. (Clinical and Experimental Metastasis, 1995 Vol. 13:296-302, Applicant's reference AJ on the Information Disclosure Statement filed September 19, 2003).

Claims 1, 2, 4, 5, 11, 12, 13, and 14 are as described above in the 35 U.S.C. 102(b) rejections as being anticipated by either McGuire et al. or Morrissey et al.

Wilhelm et al. disclose an 18 base paired phosphorothioate oligonucleotide complementary to the urokinase plasminogen activator transcript starting at nucleotide position –10 upstream of the AUG initiation codon, and an 18 base paired phosphorothioate oligonucleotide complementary to the first 18 bases downstream of the AUG translation initiation codon (see page 297, second column). It is noted that prior to experiments, the phosphorothioate oligonucleotides were reconstituted in sterile water and thus constitutes a pharmaceutically acceptable carrier or diluent. It is further noted that ovarian cancer cells in culture were administered with the phosphorothioate oligonucleotides together with a liposome formulation and thus constitutes a colloidal dispersion system.

Therefore Wilhelm et al. anticipate claims 1, 2, 4, 5, 11, 12, 13, and 14.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and 4-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilhelm et al. (Clinical and Experimental Metastasis, 1995 Vol. 13:296-302, Applicant's reference AJ on the Information Disclosure Statement filed September 19, 2003) in view of Baracchini et al. [U.S. Patent No. 5801154].

Claim 1 is drawn to a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase plasminogen activator. Claims 2, 4-10, and 12-14 are dependent on claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound is an antisense oligonucleotide; wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage; wherein the modified internucleoside linkage is a phosphorothioate linkage; wherein the antisense oligonucleotide comprises at least one modified sugar moiety; wherein the sugar moiety is a 2'-O-methoxyethyl sugar moiety; wherein the antisense oligonucleotide comprises at least one modified nucleobase; wherein the modified nucleobase is a 5-methylcytosine; wherein the antisense oligonucleotide is a chimeric oligonucleotide; and a composition comprising a compound targeted to a nucleic acid

molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase plasminogen activator and a pharmaceutically acceptable carrier or diluent, and further comprises a colloidal dispersion system; and wherein the compound is an antisense oligonucleotide. Claim 11 is drawn to a compound which specifically hybridizes with at least an 8-nucleobase portion of an active site on a nucleic acid molecule encoding urokinase plasminogen activator.

Wilhelm et al. teach an 18 base paired phosphorothioate oligonucleotide complementary to the urokinase plasminogen activator transcript starting at nucleotide position –10 upstream of the AUG initiation codon, and an 18 base paired phosphorothioate oligonucleotide complementary to the first 18 bases downstream of the AUG translation initiation codon (see page 297, second column). It is noted that prior to experiments, the phosphorothioate oligonucleotides were reconstituted in sterile water and thus constitutes a pharmaceutically acceptable carrier or diluent. It is further noted that ovarian cancer cells in culture were administered with the phosphorothioate oligonucleotides together with a liposome formulation and thus constitutes a colloidal dispersion system.

Wilhelm et al. do not teach wherein the antisense oligonucleotide comprises at least one modified sugar moiety, at least one modified nucleobase, or wherein the antisense oligonucleotide is a chimeric oligonucleotide.

Baracchini et al. teach modified or substituted oligonucleotides are often preferred over native forms because of desirable properties such as enhanced cellular

uptake, enhanced affinity for nucleic acid target and increased stability in the presence of nucleases. Baracchini et al. further teach antisense oligonucleotides with at least one modified sugar moiety, such as a modified 2'-O-methoxyethyl sugar moiety (see Table I); or with modified nucleobases, such as 5-methylcytosine (see column 7, lines 15-25). Baracchini et al. also teach an antisense oligonucleotide as a chimeric oligonucleotide (see column 8, lines 12-19).

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to make a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase plasminogen activator as taught by Wilhelm et al. One of ordinary skill in the art would have been motivated to make a compound targeted to a nucleic acid molecule encoding urokinase plasminogen activator, wherein said compound specifically hybridizes with and inhibits the expression of urokinase plasminogen activator for the purpose of reducing the spread of human ovarian cancer in mice as taught by Wilhelm et al.

It would have been obvious to one of ordinary skill in the art to modify the antisense oligonucleotide targeting urokinase plasminogen activator with various modifications and substitutions, including a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase following the methods of Baracchini et al. One of ordinary skill in the art would have been motivated to modify the antisense oligonucleotides since the prior art has taught the desirability of such oligonucleotides are often preferred over native forms because of increased stability in the presence of

nucleases (see Baracchini et al.). One of ordinary skill in the art would have expected success at modifying the antisense oligonucleotide since Baracchini et al. taught the successful design and synthesis of modified antisense oligonucleotides and their use for inhibiting gene expression in cultured cells.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
May 1, 2006